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DT07 Rec'd PCT/PTO 29 NOV 2004

PATENT  
0283-0200PUS1

IN THE U.S. PATENT AND TRADEMARK OFFICE

Applicant: MIYATA et al. Conf.: UNASSIGNED  
Appl. No.: 10/510,483 ✓ Group: UNASSIGNED  
Filed: October 7, 2004 Examiner: UNASSIGNED  
For: PROCESSES FOR PREPARING EITHER OPTICALLY  
ACTIVE N-SUBSTITUTED BETA-AMINO ACID AND  
OPTICALLY ACTIVE N-SUBSTITUTED BETA-  
AMINO ACID ESTER OR OPTICALLY ACTIVE N-  
SUBSTITUTED 2-HOMOPIPECOLIC ACID AND  
OPTICALLY ACTIVE N-SUBSTITUTED 2-  
HOMOPIPECOLIC ACID ESTER

L E T T E R

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

NOV 29 2004

Sir:

Subsequent to the filing of the above-identified application on October 7, 2004, attached hereto is an English translation of the International Preliminary Examination Report (IPER 409) that should be made of record in the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 

John W. Bailey, #32,881

JWB:enm  
0283-0200PUS1

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Attachment(s)

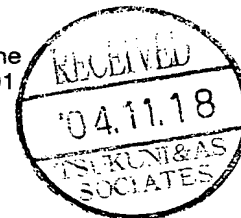
From the INTERNATIONAL BUREAU

**PCT**

**NOTIFICATION OF TRANSMITTAL  
OF COPIES OF TRANSLATION  
OF THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**  
(PCT Rule 72.2)

To:

TSUKUNI, Hajime  
SVAX TS Bldg.  
22-12, Toranomon 1-chome  
Minato-ku, Tokyo 105-0001  
JAPON



Date of mailing (day/month/year) 11 November 2004 (11.11.2004)	
Applicant's or agent's file reference FP2569PCT	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/JP2003/004437	International filing date (day/month/year) 08 April 2003 (08.04.2003)
Applicant UBE INDUSTRIES, LTD. et al	

**1. Transmittal of the translation to the applicant.**

The International Bureau transmits herewith a copy of the English translation made by the International Bureau of the international preliminary examination report established by the International Preliminary Examining Authority.

**2. Transmittal of the copy of the translation to the elected Offices.**

The International Bureau notifies the applicant that copies of that translation have been transmitted to the following elected Offices requiring such translation:

AZ, CA, CH, CN, CO, EP, GH, KG, KP, KR, MK, MZ, RO, RU, TM

The following elected Offices, having waived the requirement for such a transmittal at this time, will receive copies of that translation from the International Bureau only upon their request:

AE, AG, AL, AM, AP, AT, AU, BA, BB, BG, BR, BY, BZ, CR, CU, CZ, DE, DK, DM, DZ, EA, EC, EE, ES, FI, GB, GD, GE, GM, HR, HU, ID, IL, IN, IS, JP, KE, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MN, MW, MX, NI, NO, NZ, OA, OM, PH, PL, PT, SC, SD, SE, SG, SK, SL, TJ, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

**3. Reminder regarding translation into (one of) the official language(s) of the elected Office(s).**

The applicant is reminded that, where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report.

**It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned (Rule 74.1). See Volume II of the PCT Applicant's Guide for further details.**

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.+41 22 740 14 35	Authorized officer  Yoshiko Kuwahara  Facsimile No.+41 22 338 90 90
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Translation

PATENT COOPERATION TREATY

PCT/JP2003/004437



# PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference FP2569PCT	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/JP2003/004437	International filing date (day/month/year) 08 April 2003 (08.04.2003)	Priority date (day/month/year) 08 April 2002 (08.04.2002)
International Patent Classification (IPC) or national classification and IPC C12P 41/00		
Applicant UBE INDUSTRIES, LTD.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.  <input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).  These annexes consist of a total of _____ sheets.
3. This report contains indications relating to the following items:  I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 25 September 2003 (25.09.2003)	Date of completion of this report 14 May 2004 (14.05.2004)
Name and mailing address of the IPEA/JP	Authorized officer
Facsimile No.	Telephone No.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP2003/004437

## I. Basis of the report

### 1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☐ the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the claims:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, as amended (together with any statement under Article 19  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the drawings:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_
- ☐ the sequence listing part of the description:  
 pages \_\_\_\_\_, as originally filed  
 pages \_\_\_\_\_, filed with the demand  
 pages \_\_\_\_\_, filed with the letter of \_\_\_\_\_

### 2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

### 3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

### 4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages \_\_\_\_\_
- ☐ the claims, Nos. \_\_\_\_\_
- ☐ the drawings, sheets/fig \_\_\_\_\_

### 5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rule 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/JP03/04437

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims	1-10	YES
	Claims		NO
Inventive step (IS)	Claims		YES
	Claims	1-10	NO
Industrial applicability (IA)	Claims	1-10	YES
	Claims		NO

## 2. Citations and explanations

Document 1: JP 10-33191 A (Mitsubishi Rayon Co., Ltd.) February 10, 1998,  
Full text, especially Claims; Par. No 0028; and Examples (Family: none)

Document 2: Shun-Ichi Murahashi et al. "A Novel Oxidative Ring-Opening of Isoxazolidines: Syntheses of  $\beta$ -Amino Ketones and  $\beta$ -Amino Acid Esters from Secondary Amines," Tetrahedron Letters, 1988, Vol. 29 (49), p. 5949-5952, Full text, especially Table 2

Document 3: US 5928933 A (E. I. du Pont de Nemours & Company) July 27, 1999  
Full text (Family: none)

Document 4: EP 144980 A1 (LONZA AG) June 19, 1985,  
Full text & JP 60-139655 A & US 4585887 A

Document 5: WO 95/18134 A1 (Asymmetry Limited) July 6, 1995  
Full text & EP 736031 B1 & JP 9-507221 & US 6037498 A

Document 1 describes a process for producing optically active 3-N substituted amino isobutyric acids characterized by asymmetric hydrolysis of the racemic 3-N substituted amino isobutyric acid ester represented in Formula (2) in the presence of an asymmetric ester-hydrolyzing enzyme. It also lists lipases, proteases, and esterases from microorganisms such as *Candida antarctica*, etc., as the asymmetric ester-hydrolyzing enzyme. It also states that the reaction is carried in a system that contains not only an aqueous medium but also an organic solvent such as an ether or an aromatic or aliphatic hydrocarbon solvent as the reaction medium. More specifically, it states that the racemic 3-acetyl amino isobutyric acid methyl ester was added to a suspension of *E. coli*, asymmetric hydrolysis was performed, and optically active 3-acetyl amino isobutyric acid methyl ester and optically active 3-acetyl amino isobutyric acid were obtained.

Document 2 describes  $\beta$ -amino butyrates, and the specific compounds are shown as the Product in Entry 1 and 5 of Table 2.

Document 3 states that lipase from *Candida antarctica* is used for asymmetric hydrolysis.

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International Application No.

PCT/JP03/04437

## Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

## Continuation of Box V:

Document 4 describes diastereomer N-substituted amino acid ester hydrochlorides, and it states that optically active 3-aminocarboxylic acid esters are obtained by hydrolysis. More specifically, a 3-(1'-methylbenzylamino)-butanoic acid ester diastereomer is produced.

Document 5 describes the secondary amine represented by Formulas (IIIa) and (IIIb).

Based on the descriptions in documents 1-5, the inventions of claims 1-10 lack an inventive step.

As described in document 1, the asymmetric hydrolysis of racemic 3-N substituted amino isobutyric acid ester in the presence of an asymmetric ester-hydrolyzing enzyme was publicly known before the priority date of this application, and because it is clear that N-substituted- $\beta$ -amino acid alkyl esters have the kind of asymmetric carbon atoms described in documents 2, 4, and 5 depending on the positions of their substituents, this examination finds that persons skilled in the art can easily conceive of a process for producing optically active N-substituted- $\beta$ -amino acid alkyl esters and N-substituted- $\beta$ -amino acids by asymmetric hydrolysis of the N-substituted- $\beta$ -amino acid alkyl esters described in document 1. In addition, this examination finds that persons skilled in the art can easily conceive of using the lipase from *Candida antarctica* described in document 3 as the asymmetric hydrolyzing enzyme.

As a result, this examination finds that persons skilled in the art can easily conceive of the inventions of claims 1-10 based on the descriptions in documents 1-5.